REMARKS/ARGUMENTS

With entry of this amendment, claims 67-80 and 82-84 are pending in this application. The specification is amended to update the priority information as well as to correct certain obvious typographical errors. In addition, claim 80 is canceled without prejudice or disclaimer, and claims 67 and 72-77 are amended as set forth in detail below. No new matter is added. Applicants reserve the right to pursue any canceled subject matter and/or claims of original scope in related, co-pending application. In view of these amendments and the remarks below, reconsideration of the present application is respectfully requested.

Amendments to the Specification

The specification has been amended to update the priority information by specifying the current status of U.S. Application No. 09/451,489 as "issued." In addition, the specification has been amended to correct an obvious typographical error at page 3, line 1, by deleting "r," from the recitation of "... marker, r, survival ...." The specification has also been amended to correct an obvious typographical error at page 23, line 9, by substituting "BRDU" for "BRU." No new matter is added by these amendments.

Claim Amendments

Independent claim 67 has been amended to recite an embodiment of the present invention with greater particularity by specifying that the fish is a "teleost." Support for this amendment is found in the application as filed at, *e.g.*, page 7, line 31. Corresponding amendments have been made as appropriate in the dependent claims.

Claim 73 has been amended for greater clarity to recite "wherein the cell or the population of cells are microinjected into [[the]] a blastula ~~of the~~ stage embryo."

Claim 81 has been canceled without prejudice or disclaimer.

No new matter is added by these amendments. There amendments are made for purposes of further expediting prosecution of this application and should not be construed as acquiescence to any rejection.

Priority

The specification has been amended to update the priority information in the first sentence by specifying that U.S. Application No. 09/451,489 has "issued as U.S. Patent No. 6,761,876." In view of this amendment, Applicants respectfully request withdrawal of the present objection under 37 C.F.R. § 1.78(a)(2) and (a)(5).

Specification

The Examiner has objected to the specification because of two obvious typographical errors: page 3 at line 1 reads "...markers, r, survival..." and page 23 at line 9 reads "BRU" instead of "BRDU." The specification has been amended to correct these obvious errors. Accordingly, withdrawal of the present objection is respectfully requested.

Rejections Under 35 U.S.C. § 112, first paragraph

Enablement

Claims 67-76 and 78-83

Claims 67-76 and 78-83 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly not enabled by the specification. The Examiner contends that, while the claims are enabled for oviparous fish species, the claims are not enabled for any viviparous fish species. The Examiner also alleges that the claims are not enabled for determining the presence of a pathogen in a sample. In particular, the Examiner states that the specification does not "teach or even contemplate how to transplant cells comprising a pathogen without causing death of the

embryo or how one would detect a pathogen." This rejection is traversed in part and overcome in part as set forth below.

First, with regard to enablement of oviparous fish species, in order to further expedite prosecution of the instant application, Applicants have amended the present claims to specify a "teleost" embryo. Applicants note that the Examiner has acknowledged enablement of the present claims with respect to oviparous fish species. Accordingly, because teleosts are a family of oviparous fish, Applicants believe this aspect of the present rejection to be obviated by the present amendments.

As to transplanting and detecting pathogens, Applicants disagree with the Examiner's contention that such embodiments are not enabled by the specification. Whether a specification would have been enabling as of the filing date involves "consideration of the nature of the invention, the state of the prior art, and the level of skill in the art." MPEP § 2164.05(a). Thus, to provide an enabling disclosure, a specification "need not disclose what is well-known to those skilled in the art and preferably omits that which is well-known to those skilled and already available to the public." *Id.* (citing *In re Buchner*, 18 USPQ2d 1331, 1332 (Fed. Cir. 1991)). *See also Falkner v. Inglis,* 79 USPQ2d 1001, 1006 (Fed. Cir. 2006).

In the present case, the claims are directed to a method of analyzing a sample for presence of a cancer cell or pathogen comprising, *inter alia*, introducing a cell or population of cells, the cells having been obtained from a patient, into a teleost embryo, and detecting a property of the cell or the population of cells to indicate whether the cell or the population of cells comprises a cancer cell or pathogen. Accordingly, the nature of the invention relates generally to detection of a cancer cell or pathogen. In this regard, techniques for detecting pathogens were already generally well-known in the art. Such methods included, for example, visualization by microscopy and/or detection of a specific signal associated with a pathogen (*e.g.*, via the use of specific antibodies, nucleic acid probes, or reporter constructs), to name a few. The skilled artisan reading the specification would thus readily recognize that such known techniques could be used in accordance with the presently claimed method, in which the cells or

populations of cells have been introduced into a teleost embryo. Therefore, it is not necessary that Applicants recite such known techniques in the application itself.

As to the Examiner's assertion that the specification does not teach "how to transplant cells comprising a pathogen without causing death of the embryo," there is no requirement in the claims that the recipient fish survive the transplantation procedure indefinitely. It is only required that a skilled artisan be able to detect a property of the transplanted cell(s) so as to indicate whether a pathogen is present. The specification teaches, *inter alia*, that heterologous cells, including cells or populations of cells comprising a pathogen, can be transplanted into fish embryos, and that the introduced heterologous cells typically remain viable "for a period sufficient to conduct various analyses ... (for example, at least an hour and typically at least a day, and sometimes up to three days, a week or longer)." (Specification at p. 7, ll. 21 & 22.) The skilled artisan would understand such a time period as being sufficient for detecting a property of the cell or the population of cells to indicate the presence of a pathogen, as well as for amplification of a pathogen, as presently recited in the claims. Thus, even if transplantation of cells comprising a particular pathogen were to ultimately result in lethality in the fish recipient, the skilled artisan, reading the specification as of its filing date, would still readily accept that the transplanted cells would remain viable for a sufficient period so as to allow for detection of the pathogen.

In this regard, Applicants also emphasize that the Examiner bears the initial burden of providing evidence or reasoning why a pending claim does not meet the enablement requirement of 35 U.S.C. § 112, first paragraph. The CCPA has stated the following with respect to the Examiner's burden:

> a specification disclosure which contains a teaching of how to use the claimed invention in terms which correspond in scope to those used in the claims *must* be taken as in compliance with the [enablement requirement of § 112, first paragraph,] *unless* there is reason to doubt the objective truth of the statements contained therein .....

In re Marzocchi, 169 USPQ 367, 369 (CCPA 1971) (emphasis original); *see also* MPEP § 2164.04. It is incumbent upon the Examiner to explain why the truth or accuracy of these statements should be doubted and to provide acceptable evidence or reasoning in support. *See Marzocchi*, 169 USPQ at 370. In the present case, the Examiner has not provided any reasoning or evidence to establish non-enablement of the present claims as they pertain to transplantation of a cell or population of cells comprising a pathogen.

While the present claims are enabled by the specification for at least the reasons above, as further evidence of enablement and in the interest of compact prosecution, Applicants have submitted herewith Exhibit A (Davis *et al.*, *Immunity* 17:693-702, 2002; hereinafter "Davis"). Davis demonstrates the use of the zebrafish embryo as a model for studying *Mycobacterium*-macrophage interactions. (*See* Davis at, *e.g.*, Abstract.) As described in Davis, pathogenic Mycobacteria (*M. marinum*) were introduced into early embryonic stage zebrafish. (*See id.* at, *e.g.*, p. 694, 2nd col., bridging to p. 695, 1st col. (describing introduction of *M. marinum* bacteria into zebrafish at either 5 hr or 32 hr post-fertilization).) Embryos injected with a relatively high dose of pathogen (> 500 *M. marinum*) remained viable for at least 6-9 days postinfection (*see id.* at p. 695, 2nd col., 1st full para.), whereas most embryos injected with a relatively low dose (< 20 bacteria) survived during the entire 9 day monitoring period (*see id.*). Furthermore, bacteria were detected in infected embryos using either fluorescence or Differential Interference Contrast (DIC) microscopy (*see id.* at, *e.g.*, p. 694 (Figure 1) and p. 695 (Figure 2)), microscopic methods well-known in the art as of the effective filing date of the application. Pathogen was detected in infected embryos as soon as 1 hour postinfection (*see id.* at p. 694 (Figure 1C)). Thus, as evidenced by Davis, zebrafish embryos, into which pathogenic cells have been introduced, remain viable for a sufficient period of time (at least an hour and up to a week or longer, as described in the as-filed application) to allow detection of the pathogenic cells using detection methods well-known in the art.

For at least the reasons and amendments set forth above, Applicants believe the present claims are enabled by the specification under 35 U.S.C. § 112, first paragraph. Withdrawal of the present rejection is respectfully requested.

Claims 77 and 84

Claims 77 and 84 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabled, the Examiner asserting that these claims limit the scope of claim 67 to non-enabled embodiments (analysis for the presence of a pathogen, as previously discussed above). Because the claims are enabled with respect to analysis for the presence of a pathogen, as set forth above, claims 77 and 84 are also enabled. Accordingly, withdrawal of the present rejection is respectfully requested.

Written Description

Claim 81 stands rejected under 35 U.S.C. § 112, first paragraph, as allegedly not complying with the written description requirement. In particular, the Examiner believes that dyes specifically taken up by cancer cells lacks written description. While not agreeing with this rejection, Applicants note that the rejection is obviated by the cancellation of claim 81, as previously set forth.

Rejections Under 35 U.S.C. § 112, second paragraph

Claim 73 stands rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite. The Examiner states that claim 73 is "unclear because it requires injection into the blastula of the embryos," and that it is "not clear if the claim is referring to a specific part of the embryo or if it is referring to the blastula stage embryo."

Applicants believe that the skilled artisan, reading claim 73 in light of the specification and the contemporary knowledge in the art, would reasonably understand the recitation of "the blastula of the embryo" as referring to a blastula stage embryo. For this reason, Applicants believe claim 73 is definite. In any event, for purposes of further expediting prosecution of this application, claim 73 has been amended for further clarity, as previously set forth, to read "microinjected into a blastula stage embryo," as suggested by the Examiner.

In view of the remarks and amendments set forth above, withdrawal of the present rejection is respectfully requested.

Double Patenting Rejection

Claim 83 stands rejected on the ground of nonstatutory obviousness-type double patenting as allegedly unpatentable over claims 1, 33, 40, and 16 of U.S. Patent No. 6,761,876. Applicants will consider the need for filing an appropriate terminal disclaimer upon an indication of otherwise allowable subject matter.

CONCLUSION

In view of the foregoing, Applicants believe all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 206-467-9600.

Respectfully submitted,

Dated: February 14, 2007

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